

Docket No.: NEB-214-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Xu et al. EXAMINER: Venci, D.

SERIAL NO.: 10/733,617 GROUP: 1641

FILED: December 11, 2003

FOR: Immobilized Peptide Carrier Conjugates and Uses
Thereof

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

VIA EFS WEB: WWW.USPTO.GOV

Sir:

RESPONSE TO INTERVIEW SUMMARY

This is in response to the Interview Summary dated February 29, 2008. The Interview Summary was presented after a telephone interview of February 8, 2008. The purpose of the interview was to assist the Examiner in understanding the claimed invention as discussed in the response to Final Office Action dated November 14, 2007. In particular, Applicants Drs. Evans and Xu together with their representative Dr. Strimpel explained to the Examiner and Supervisory Examiner Long Le the content of the Table on page 11 of the response. In so doing, Applicants drew attention to the significance of having a C-terminal thioester on the carrier (anchor) molecule instead of the ligand described by Knock et al.

In the telephone conference, Applicants further explained to the Examiner and Supervisory Examiner Le the intein-mediated cleavage mechanism described in the prior art. In this context, the published paper provided by Applicants in the response to the final office action dated November 14, 2007 was discussed (Evans et al. *Protein Science* 7:2256-2264 (1998)).

The present claimed invention describes a use of intein-mediated cleavage for purification procedures. The purification procedure requires a thioester at the C-terminus of a carrier protein, where the carrier protein is capable of both covalent attachment to a selected ligand through the C-terminal thioester and non-covalent linkage to a matrix. Once covalently attached, the ligand is capable of purifying a ligand-binding molecule. The ligand can be any protein or small molecule having a nucleophilic group for binding to the thiol group on the carrier. Importantly, unlike Knock et al., the ligand is not limited to a protein.

This purification procedure is also quite distinct from the Cantor et al. reference cited by the Examiner in the Advisory Action dated December 27, 2007 and discussed in the telephone interview of February 8, 2008.

To reiterate the telephone conference of February 8, 2008, the Cantor et al. reference describes release of a target protein. The claimed invention describes immobilization of a ligand.

The Cantor et al. reference shows a fusion protein consisting of a chitin-binding domain fused to an intein which is fused to an extein.

Extein-CO-S-intein-CBD-matrix (Cantor et al.)

In the presence of DTT, the extein is released via the formation of a thioester on the extein. The result is HS-intein-CBD-matrix + extein-CO-DTT. The extein is then purified. The intein-mediated cleavage is the last step of the release procedure.

The thioester in the second cartoon of Figure 1 of Cantor et al. is internally positioned between the intein and the extein. It is not a C-terminal thioester as claimed.

The present claimed invention requires an immobilized carrier having a C-terminal thioester that is formed as a result of intein cleavage. Prior to intein cleavage, the fusion protein has the molecular structure: Intein-S-CO-CBD, which is the mirror image with respect to the matrix of the Cantor et al. structure. Intein cleavage is an initial step. The mirror image of the bonds between intein and carrier in the present claimed method compared with Cantor et al. results in significantly different consequences.

Intein-S-CO-carrier-matrix + MESNA \Rightarrow $\text{SO}_3\text{CH}_2\text{CH}_2\text{S-CO-}$
carrier matrix (Applicant) .

The C-terminal thioester on the carrier after MESNA-induced intein-mediated cleavage is particularly suitable to react with a molecule with a nucleophilic group.

With respect to the above, the Examiner has agreed to withdraw the finality of the Office Action dated November 14, 2007 (making the Advisory Action moot) and issue a new non-final rejection. The Examiner has informed the Applicant that the clock has stopped on the Notice of Appeal dated November 14, 2007.

Applicants look forward to responding to any additional issues or concerns of the Examiner and allowance of the claims.

CONCLUSION

For the reasons set forth above, Applicants respectfully request that the finality of the Office Action mailed November 14, 2007 be withdrawn and submit that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited.

Applicants believe that no fees are due at this time. However, Applicants authorize that any deficiencies that may be due be charged to Deposit Account No. 14-0740.

Respectfully submitted,

NEW ENGLAND BIOLABS, INC.

Date: March 18, 2008

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